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Kaoru Miyamoto

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01/05/2010

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EXAMINER

DUNSTON, JENNIFER ANN

ART UNIT

PAPER NUMBER

1636

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/534,424

Applicant(s)

MIYAMOTO ET AL.

Examiner

Jennifer Dunston

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2009.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 7, 8, 12 and 13 is/are pending in the application.
4a) Of the above claim(s) 7, 8 and 12 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1 and 13 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 10 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☒ Other: Appendices I-III

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 9/2/2009, in which claim 1 was amended. Claims 1, 7, 8, 12 and 13 are pending.

Any rejection of record in the previous office actions not addressed herein is withdrawn. New grounds of rejection are presented herein that were not necessitated by applicant's amendment of the claims since the office action mailed 4/2/2009. Therefore, this action is not final.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 8/2/2007 is acknowledged.

Claims 7, 8 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/2/2007.

Claims 1 and 13 are under consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by UniProt Accession NO. Q9H4I2 (publicly available June 2002). This is a new rejection.

Regarding claims 1 and 13, Q9H4I2 teaches the sequence of instant SEQ ID NO: 1 (See the attached alignment in Appendix I).

Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of the claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 U.S.C. 102, or "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, the protein taught by Q9H4I2 is identical to the protein of SEQ ID NO: 1 and would necessarily have the same function.

Response to Arguments - 35 USC § 102

The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Ishikawa et al has been withdrawn in view of Applicant's amendment to the claim in the reply filed 9/2/2009.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al (WO 01/57190 A2, cited in a prior action; see the entire reference) in view of GenBank Accession No. BAA23691.2 (GI: 20521029, May 2002, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 4/2/2009 and is reiterated below.

Tang et al teach that isolated polypeptides are separated from their natural source and contain, if anything, only a solvent, buffer, ion, or other component present in solution (e.g., page 11, lines 19-24). Tang et al teach an isolated polypeptide of SEQ ID NO: 1479 (e.g., page 28, lines 9-11). Further, Tang et al teach that the sequence of disclosed polypeptides may be modified by substitution of a selected amino acid residue in the coding sequence (e.g., page 31, lines 1-9). Moreover, Tang et al teach that methods of determining the identity and/or similarity of two polypeptides are known in the art (e.g., page 33, lines 1-15). Tang et al teach that guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest may be found by comparing the sequence of the particular

polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology or by replacing amino acids with a consensus sequence (e.g., page 10, lines 9-15).

The amino acid sequence of SEQ ID NO: 1479 is 956 amino acids in length and 99.9% identical to the amino acid sequence of SEQ ID NO: 1 (see the attached alignment in Appendix II). The only difference between SEQ ID NO: 1479 of Tang et al and instant SEQ ID NO: 1 is that it contains an asparagine residue at position 310, rather than a serine residue.

Tang et al do not teach a composition comprising a protein consisting of SEQ ID NO: 1, because position 310 is an asparagine residue.

GenBank Accession No. BAA23691.2 teaches the amino acid sequence of the KIAA0395.

It would have been within the skill of the art at the time the invention was made for the ordinary artisan to align the sequence of Tang et al with the sequence of GenBank Accession No. BAA23691.2. Sequence alignment is taught by Tang et al (e.g., page 31, lines 1-9). An alignment of the sequence of Tang et al and GenBank Accession No. BAA23691.2 is provided in Appendix III. Tang et al teach that it is within the skill of the art to make single amino acid substitutions based upon a sequence comparison with a homologous peptide. Because GenBank Accession No. BAA23691.2 teaches a homologous peptide with a serine at position 310 of the amino acid sequence of SEQ ID NO: 1479 of Tang et al, it would have been within the skill of the art at the time the invention was made to replace the asparagine at position 310 with a serine in order to achieve the predictable result of providing a functional protein by substituting one naturally occurring amino acid for another.

Response to Arguments - 35 USC § 103

With respect to the rejection of claims 1 and 13 under 35 U.S.C. 103(a) as being unpatentable over Tang et al (WO 01/57190 A2) in view of GenBank Accession No. BAA23691.2, Applicant's arguments filed 9/2/2009 have been fully considered but they are not persuasive.

The response asserts that Tang et al alone or in view of GenBank Accession No. BAA23691.2 does not teach or suggest a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein as an effective component having an amino acid sequence of SEQ ID NO: 1, wherein the protein comprises amino acids 1-107 and 242-555 of SEQ ID NO: 1 and has at least 85% sequence identity to SEQ ID NO: 1, wherein the gene is a type II hexokinase or a pyruvate kinase M gene, as presently recited in present claim 1. Further, the response asserts that Tang et al alone or in view of GenBank Accession No. does not teach or suggest a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein consisting of amino acid sequence SEQ ID NO: 1 as an effective component, wherein the gene is a type II hexokinase or a pyruvate kinase M gene, as recited in claim 13.

These arguments are not found persuasive. Tang et al teach a protein that is 99.9% identical to instant SEQ ID NO: 1. This protein is almost identical to SEQ ID NO: 1 and would be expected to have the same function as the protein of instant SEQ ID NO: 1. Furthermore, the combined teachings of Tang et al and GenBank Accession No. BAA23691.2 result in a protein that is 100% identical to instant SEQ ID NO: 1. Because the protein is 100% identical to SEQ

ID NO: 1 it will necessarily have the same function. In response to applicant's argument that the references do not teach repression of transcription of type II hexokinase gene or pyruvate kinase M gene in hepatoma cells, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

The response asserts that the Patent Office has made no more than a conclusory assertion that the cited references can be combined without articulating a reason with some rational underpinning to support the legal conclusion of obviousness.

This argument is not found persuasive. The rejection of record explains that Tang et al teach an isolated polypeptide of SEQ ID NO: 1479 (e.g., page 28, lines 9-11). Further, Tang et al teach that the sequence of disclosed polypeptides may be modified by substitution of a selected amino acid residue in the coding sequence (e.g., page 31, lines 1-9). Moreover, Tang et al teach that methods of determining the identity and/or similarity of two polypeptides are known in the art (e.g., page 33, lines 1-15). Tang et al teach that guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest may be found by comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology or by replacing amino acids with a consensus sequence (e.g., page 10, lines 9-15). The amino acid sequence of SEQ ID NO: 1479 is 956 amino acids in length and 99.9% identical to the amino acid sequence of SEQ ID NO: 1 (see the attached alignment in Appendix II). The only difference between SEQ ID NO: 1479 of Tang et al and instant SEQ ID NO: 1 is that it contains

an asparagine residue at position 310, rather than a serine residue. GenBank Accession No. BAA23691.2 teaches the amino acid sequence of the KIAA0395. Accordingly, it would have been within the skill of the art at the time the invention was made for the ordinary artisan to align the sequence of Tang et al with the sequence of GenBank Accession No. BAA23691.2. Sequence alignment is taught by Tang et al (e.g., page 31, lines 1-9). An alignment of the sequence of Tang et al and GenBank Accession No. BAA23691.2 is provided in Appendix III. Tang et al teach that it is within the skill of the art to make single amino acid substitutions based upon a sequence comparison with a homologous peptide. Because GenBank Accession No. BAA23691.2 teaches a homologous peptide with a serine at position 310 of the amino acid sequence of SEQ ID NO: 1479 of Tang et al, it would have been within the skill of the art at the time the invention was made to replace the asparagine at position 310 with a serine in order to achieve the predictable result of providing a functional protein by substituting one naturally occurring amino acid for another.

The response asserts that the rejection fails to articulate why one would have been motivated to select SEQ ID NO: 1479 of Tang et al from the 3,960 sequences disclosed in Tang et al and then align it with GenBank Accession NO. BAA23691.2, and then replace the asparagine at position 310 of SEQ ID NO: 1479 with a serine. Further, the response asserts that neither reference provides motivation for why the residue at position 310 should be changed.

A suggestion or motivation to combine references is an appropriate method for determining obviousness, however it is just one of a number of valid rationales for doing so. The Court in KSR identified several exemplary rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness

as laid down in *Graham. KSR*, 550 U.S. at ___, 82 USPQ2d at 1395-97. See MPEP § 2141 and § 2143. The rejection of record is based upon the predictable substitution of one element for another in order to achieve a predictable result.

The response asserts that nowhere do Tang et al suggest that the protein of SEQ ID NO: 1479 is non-functional or that the asparagine should be changed. Further, the response asserts that the proposed modification would not have been apparent to one of ordinary skill in the art, nor would the outcome have been predictable without knowledge of the functional domain within SEQ ID NO: 1.

This argument is not found persuasive. The Examiner is not of the position that the protein of Tang et al is non-functional. The protein would be expected to be functional whether asparagine or serine was present at position 310. The art teaches the sequences of naturally occurring variants of the protein, some proteins have asparagine at position 310 and some have serine at position 310. Both proteins are expected to be functional, with either asparagine or serine at position 310. This is not unexpected given that both asparagine and serine have polar, uncharged R groups. No knowledge of any functional domain is required to make the amino acid substitution. It is not inventive to have a serine at position 310 when this amino acid is known to occur at this position in naturally occurring variants.

The response asserts that only after reviewing the instant specification would one of ordinary skill in the art be motivated to modify Tang et al as proposed.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so

long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the rejection of record only takes into consideration knowledge which was within the level of ordinary skill at the time the claimed invention was made, as evidenced by the teachings of Tang et al with regard to sequence alignment and modification.

Accordingly, a *prima facie* case of obviousness has been established, and Applicant has not provided evidence of secondary considerations sufficient to overcome the rejection.

For these reasons, and the reasons made of record in the previous office actions, the rejection is *maintained*.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

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may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Dunston/

Examiner

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